MSK.P-035-US
PATENT APPLICATION

ORIGINAL COPY OF #12

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Sadelain et al.		
Serial No.:	08/940,544	Examiner: L. Helms	
Filed:	September 30, 1997	Art Unit: 1642	
For:	Fusion Proteins of a Single-Chain Antibody and CD28 and Uses Thereof		

PRELIMINARY REMARKS

Asst. Commissioner for Patents

Washington, D.C. 20231

Sir:

Applicants filed a Request for Continued Prosecution (CPA) in connection with the above-referenced application on October 1, 2001. It is noted that this paper has not been entered in the Patent Office database as reflected in the PAIR system accessible on-line. Should an additional copy of this paper and the return receipt postcard be required, one will be provided upon request. It is noted, however, that the application has been published (Publication No. 2002-0018783-A1), and that the paper presumably has been correctly received.

In the parent application, an Official Action was mailed March 30, 2001. Claims 1-7 were considered in the parent application.

The Examiner rejected the claims for obviousness-type double patenting in view of Application Serial No. 09/142,974 in view of Alvarez-Vallina and Sambrook, and in view of Eshar, Fousar and Sambrook. As noted below, Applicants submit that the Alvarez-Vallina reference is not prior art, and therefore cannot be relied on in this context. Applicants further

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I hereby certify that this paper and the attachments named herein are being deposited with the United States Postal Service as first class mail in an envelope addressed to Asst. Commissioner for Patents, Washington, D.C. 20231 on March 15, 2002

March 15, 2002
Date of Signature

Marina T. Larson
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note that the '974 application has been allowed on February 28, 2002 with two claims which recite specific sequences.

The Examiner rejected claims 1-7 under 35 USC § 103 as obvious over the combination of Cheung et al. in view of Alvarez-Vallina (claims 1-3) and optionally Sambrook (claims 1-7). Applicants enclose a declaration under Rule 131 of inventor Michel Sadelain showing the conception and reduction to practice of the present invention prior to the effective date of either of the Cheung et al or Alvarez-Vallina et al. references. Since the notebook pages are not witnessed, Applicants also enclose an additional declaration of Dr. Chad May, who was a fellow in Dr. Sadelain's lab in 1996, corroborating the information and the relevant dates. Thus, Applicants submit that this rejection is moot and should be withdrawn.

The Examiner rejected claims 1-2 as anticipated by Alvarez-Vallina. Applicants submit that this rejection is rendered moot by the Rule 131 declaration and should be withdrawn.

The Examiner rejected claims 1-2 under 35 USC § 102(b) as anticipated by Eshar et al. Eshar contains minimal examples, none of which relate to CD28 containing fusions. The Patent Office and the courts have advanced the policy that disclosure of partial nucleotide sequences and a method of how to proceed from there, even if enabling, is not sufficient to provide written description support for certain types of biotechnology inventions. The Eshar reference does not even provide this level of teaching with respect to the CD28 fusions. Instead, it says only that other fusions besides the exemplified γ and ζ-containing fusions can be made, and includes CD28 as one of a list of possible choices.

It is well established that, for anticipation, a reference must be enabling and describe the applicant's claimed invention sufficiently to have placed it in **possession** of a person of ordinary skill in the field of the invention. *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990). Otherwise, the eventual inventor of the transporter would find themselves anticipated by Star Trek. Similarly, the standards being applied to biotechnology inventions may require actual reduction to practice to establish that an applicant was in actual **possession** of the invention. Applicants respectfully submit that a reference which fails to demonstrate that a reference which fails to meet this second standard of showing **possession** of the invention which is later being claimed by another can not be held to anticipatory with respect to those claims.

Application of this concept in this case clearly comports with fundamental fairness. The actual examples in Eshar relate to fusions containing two types of T-cell receptor (TCR) chains. These receptors are involved in generating an activation signal based on interaction with adjacent chains that physiologically associate with the TCR. In contrast, CD28 must interact with a ligand (B7) displayed on B cells and other professional antigen presenting cells or dendritic cells and macrophages, and produces a multiplicity of effects. Without actually making such fusions and performing experiments, one could not know whether or not the expressed CD28 (assuming a given fusion provided expression) would associate with supramolecular complexes as does the native protein, nor could it be known whether of not the CD28 fusion would provide all of the functionality of native CD28. For these reasons, Applicants submit that Eshar neither showed that he was in possession of the invention as claimed nor placed the public in possession of the invention as claimed. Thus, the anticipation rejection based on Eshar should not be repeated.

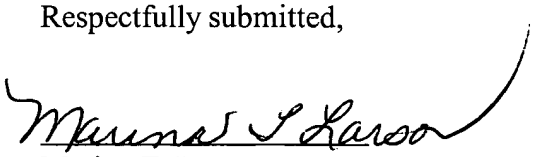
The Examiner also rejected claims 1-7 as obvious over the combination of Eshar with Fousar and Sambrook. Although Applicants acknowledge that a non-enabling reference may be used as part of an obviousness rejection, even where it is insufficient for an anticipation rejection (See, e.g., *Symbol Technologies Inc. v. Opticon Inc.,* 19 USPQ2d 1241 (Fed. Cir. 1991)), the extent of the disclosure and enablement are nonetheless relevant to the question of what is suggested. In this regard, Applicants point out that claims are directed to compositions. It appears, however, that what the Examiner has found to be obvious from the combination of references is a methodology which might be tried, and not the results, since one could not predict with reasonable certainty the characteristics of the product which would result from combining the methodology of Eshar with the secondary references. Thus, the rejection is akin to that which was reversed in *In re Kratz*, 201 USPQ 71 (CCPA 1979), where the obviousness of the methodology used to identify a compound was found not to be reason to reject the compound itself as obvious. Neither the identity of the compound nor its properties could be predicted beforehand. The same is true here.

Furthermore, it should be noted that the Fouser reference provides no more certainty with respect to the results that might be obtained with a CD28 fusion. The Fouser reference merely says that cytokines can be combined or co-administered with a 3F8-type

antibody. There is no teaching of fusion proteins, and no insights into the properties of such proteins. Thus, Applicants submit that this rejection also should not be maintained.

Favorable reconsideration of the application in view of the remarks herein is respectfully requested.

Respectfully submitted,



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